THE GOLD TREATMENT OF TUBERCULOSIS.

PRELIMINARY REPORT BY THE MEDICAL RESEARCH COUNCIL.

VARIOUS gold compounds have from time to time been used in the treatment of tuberculosis. Recently a soluble complex salt of gold and sodium—namely, sodium aurithiosulphate, which has long been known to chemists, and is now made available under the trade mark of "sanocrysin"—has been introduced to therapeutics as a treatment for tuberculosis by Professor Moellgaard of Copenhagen, who has found that it has the advantage of dissociation into complex ions, so that toxicity due to free gold ions is avoided. Such toxic effects as this compound produces in tuberculous but not in normal subjects are attributed to destruction of the bacilli and increased liberation of tubercle toxins; and Professor Moellgaard has also prepared an antitoxic serum for use, when necessary, to counteract these ill effects. The results of experiments on animals and of numerous trials on human patients in some Danish hospitals have been fully described in his book on the *Chemotherapy of Tuberculosis* (autumn, 1924). Critical summaries of these results and of other work in Denmark have been published recently in the *British Medical Journal*[1] and in the *Lancet*. Clinical trials are now proceeding also in Germany and in Canada.

Professor Moellgaard very courteously gave to the Medical Research Council a full supply both of the gold salt and of the protective serum for clinical trial in England, but desired that the preparations should not be made available for general use in medicine until the results of these trials were completed. In December he and his chief clinical colleague, Dr. Secker, visited England, and made a personal communication on the subject to those who were asked to try the preparations; while Dr. Secker remained in London long enough to visit several hospitals, advise on the selection of cases, and give the observers invaluable help during the treatment of individual patients by instruction drawn from his own wide experience.

The preparations were issued by the Council, as on the similar occasion of the introduction of insulin to therapeutics, only to those who were not engaged in private practice—that is, to whole-time professors of medicine or to tuberculosis officers. The Ministry of Health was kept in close touch with the work through a liaison officer. On account of the general interest aroused by discussion of this method of treatment, the Council thinks it desirable to issue this preliminary report on the early results of cases so far treated in Great Britain, and to explain its further policy.

Work in England has been in progress for less than three months; it has not been on a large scale, but the value of the opinions formed has been enhanced by the arrangement which used several observers of small groups working at first independently of each other rather than one observer of a large group. It was evident, when the observers subsequently met in the first conference upon which this report is based, that there was so great a divergence of opinion upon the value of the drug that any single observer, relying solely on his own experience, might easily have been led to a summary opinion that would have been unduly emphatic in his judgement for or against the treatment. The report deals solely with clinical results, and does not consider the laboratory evidence for the effect of the gold salt on tubercle bacilli or infected tissues, nor that for the protective action of the specific serum.[2]

Each dose of sanocrysin was dissolved in 10 c.cm. of distilled water and injected intravenously. The usual amount was 0.5 g. for the first injection and then repeated injections of 1 g. each at intervals of about three days, unless a severe reaction on the part of the patient occurred and compelled delay until the reaction had subsided. The total amount used in any case was generally about 5 or 6 g., and the injections were rarely continued until the goal suggested by the Danish experiences was attained—namely, a final state in which the last injection produced no rise of temperature.

The specific serum, usually from horses immunized by diaplyte tubercle vaccine, though at first a weaker calf serum also received trial, was injected into the muscles in doses of 20 c.cm. Its action is supposed to be that of neutralizing the flood of tuberculous toxins liberated by the action of the gold salt on the infected tissues, and thus of lessening the general severity of the reaction to the chemotherapeutic injection. In cases with heavy tuberculous infection the serum was used either before or together with the first gold injection as a preliminary measure. In mild cases it was not used until a reaction of some severity had occurred, and in many instances it was never used at all.

EFFECTS OF THE INJECTION OF SANOCRYSIN.

Vomiting was often noticed as an immediate effect within a few minutes of the injection. In one control patient, without evidence of tuberculous disease, there was nausea and prolonged anorexia after three injections, but no rise of temperature or any other reaction. There were no other control observations of cases with fever from known causes other than tuberculosis, so that the evidence is not sufficient to ascertain whether the gold salt can be used as a test to distinguish non-tuberculous from tuberculous febrile states. In a group of five cases of pulmonary tuberculosis that were clinically mild but radiologically moderately extensive, there were slight pyrexia and trifling albuminuria, but no other features of reaction. The gold salt in amounts up to 5 or 6 g. therefore seemed to be non-toxic for patients with only slight tuberculous lesions.

Severe reactions were generally produced in cases of more extensive infection. The temperature rose within a few hours to 103° or 104°; but there was no case of hyperpyrexia or of critical fall. Vomiting often recurred, but diarrhoea was not often observed. The patient felt ill, depressed, and lost appetite. A metallic taste was sometimes complained of, and there was a tendency to ulceration of the mouth and throat. The rise of temperature lasted three or four days, but was generally less with each successive dose. After the second or third dose rashes often appeared, like those of measles or scarlet fever, and not often itching. In one case an erythematous rash persisted for a fortnight and was accompanied by an outbreak of many indolent open sores. The rashes were seen in cases where no serum had been given. They were perhaps more frequent in cases of closed tuberculous infection.

Albuminuria was a common occurrence, and in some cases exceeded 1 per cent., though it did not last long. No oedema resulted and there was no evidence of persistent renal lesions. Measurements of blood urea were not made in any of the cases of severe albuminuria. In one necropsy, where there had never been more than trifling albuminuria, 8 per cent. of the total metallic gold injected was found in the kidneys on death twenty-eight days after the last injection

[1] It may be added that a paper by Professor Moellgaard on "The theoretical basis of the sanocrysin treatment of tuberculosis" was published in the BRITISH MEDICAL JOURNAL of April 4th (p. 643). In it he fully explained the theoretical considerations which led him to employ sodium aurithiosulphate, related some of the experiments on animals he has carried out, and indicated the precautions which should be taken in the administration of the drug.—Editor, BRITISH MEDICAL JOURNAL.

[2] These matters are discussed by Professor Moellgaard in the paper published in this JOURNAL on April 4th.—Editor, BRITISH MEDICAL JOURNAL.

of sanocrysin. Gold was proved to be excreted by the bowels and by the kidneys after an injection of sanocrysin. Jaundice of a grave nature, which in the Danish experience was a very rare event, occurred in another patient who died, and a relatively large amount of gold was found on analysis of the liver.

Features strongly suggesting that the gold salt had a direct action at the site of the tuberculous infection were often seen. Thus, in the lungs a focal reaction was evidenced by local pain, a sense of tightness, and by prolonged tachypnoea. This was in at least three instances aggravated by the development of a very critical state in which the pulse became rapid and feeble and the patient so collapsed, though the temperature did not fall seriously, that great anxiety was aroused as to the chances of recovery. Except for a local increase of crepitant râles, there were no clear changes in the physical signs in the lungs during these focal reactions. Cough, however, was generally increased and sputum was at first more abundant if the patient had strength for expectoration. Subsequently both cough and sputum tended to lessen.

Headache was never intense. A general state of depression and lack of vitality, together with loss of weight, tended to develop in cases of extensive infection after a course of treatment, and this retarded subsequent recovery in the hospital wards.

Effects of the Injection of the Protective Serum.

Clinical experience varied on this point. At some hospitals nearly every patient had severe serum sickness, perhaps with its own rash and vomiting, and certainly with severe joint and muscle pains. Other observers never saw such effects. The differences were not explained by reference to any particular batch of serum, or to different effect of calf or of horse serum respectively. There were, however, no examples of dangerous anaphylactic phenomena.

It was difficult to form a clear conclusion as to the benefit of the serum. Some observers thought they had proof of its power to control albuminuria and focal reactions in the lungs, if given early and before these features became serious; others were not convinced. In general, serum was freely used for severe cases of infection. A few trials were made of the influence of the serum on the general state of a tuberculous patient apart from the use of sanocrysin, but they led to no demonstrable results.

Summary of Clinical Results.

Clinical experience in Britain has confirmed the description in Professor Moellgaard's book of the immediate effects of sanocrysin as seen in Danish hospitals. The drug does appear clinically to have a specific action on tissues infected by tubercle bacilli, and the severity of the constitutional reactions does appear to be directly related to the intensity of the tuberculous infection. Further, the drug seems to have but slight toxicity for human patients who are not infected by tuberculosis, though in this respect very few control observations have been made. On account of the severity of the reactions in the first tuberculous patients chosen for treatment, no observer at the beginning felt justified in deliberately making control observations in other febrile infections. For the same reason no one cared to begin straight away with the treatment on a large number of tuberculous cases, but each observer preferred to select three or four individual patients and proceed cautiously.

The total number of cases covered by this preliminary report is small—about thirty, of whom twenty-two definitely had tuberculous infections of the lungs. Two of the pulmonary cases died, death in one hopeless case being perhaps accelerated by the treatment, and occurring in the other unexpectedly as the result of toxic jaundice. The remaining twenty do not lend themselves to any numerical analysis. Uncomplicated pulmonary tuberculosis is a disease of which few physicians can confidently foretell the progress, upward or downward, during any given period of two or three months, which was all the time available for these preliminary observations. But it was the opinion of those observers who had had most experience in dealing with consumption that the early cases of open tuberculous infection of the lungs did show some evident improvement, though there was no dramatic benefit, such as that seen with insulin or salvarsan in their corresponding diseases. On the other hand, cases with more advanced disease did not stand the treatment well, and the condition of some of these has been made worse. The latter experience accords with that of Dr. Secker of Copenhagen. Serious cases of long standing cannot endure the treatment in its present form.

There were two cases, not included in the preceding twenty, in which most striking improvement followed at once upon the use of the drug, both the patients having lain three months in hospital previously without making any advance. One appeared to be a case of closed tuberculosis of the lung, spreading out from hilum glands, though it could not be proved that the pulmonary inflammation was caused by tubercle bacilli and not by some other smouldering infection. The other was a case of tuberculous peritonitis with an encysted collection of fluid that vanished at once upon treatment. In each instance the patient showed the rash and rise of temperature that in other proved cases of tuberculosis have followed the injection of sanocrysin. No case of pleural effusion was treated in this preliminary group because the results in this condition would not have offered any decisive evidence. Lupus of the skin, spinal caries, renal tuberculosis, and tuberculous glands are now being treated, but their progress is not sufficiently advanced to be included in this report.

The evidence, therefore, despite the relatively poor results in open pulmonary tuberculosis—and that is unhappily the commonest form of tuberculosis—is sufficiently encouraging to demand further clinical study. This is particularly so in view of the one experience common to all observers—namely, that the drug seems to exert a specific action on tuberculous tissues. The Medical Research Council expects that many months will pass after the issue of this preliminary report before any further definite conclusions can be drawn. Trial on a larger scale is now justified, and it is hoped to widen the field of work with the help of more observers. But the Council is of opinion that such further trial and extended observations are imperatively required before it can be clearly stated that this gold salt is of value in the treatment of tuberculosis and before it should be made available for general use in medical practice in Great Britain.

Summary of Clinical Observations.

The following section briefly summarizes the clinical observations at the several places where the treatment was used. In every patient radiograms of the chest were taken before, during, and after treatment.

St. Bartholomew's Hospital (Professor F. R. Fraser).

One case, aged 30. General pulmonary tuberculosis; tubercle bacilli found once. Total gold salt used, 5.25 g. Severe reaction at first, but final injection of 1 g. caused no rise of temperature. No definite change.

London Hospital (Professor A. W. M. Ellis).

Five cases of pulmonary tuberculosis, one case of tuberculous meningitis, and one non-tuberculous control. The general impression of the results was definitely unfavourable.

——, aged 17. Four years' history. Extensive pulmonary tuberculosis both lungs. General condition good; had gained 1 st. in weight. Tubercle bacilli found once during treatment. Total gold salt used, 6.5 g. in eight weeks. Severe reactions, fever, rash, ophthalmic reactions, albuminuria, loss of weight. Gradual recovery on stopping treatment to conditions very much as on admission. No change in physical signs. Result: No change.

———, aged 53. Three months' history of pleural effusion and fibrosis. General condition fair. Tubercle bacilli present on one occasion only. Total gold salt used, 2.75 g. Gold salt discontinued because of prostration, albuminuria, prolonged nausea, and anorexia. Severe serum sickness. Lost weight and has not regained it two months after cessation of treatment. Result: No improvement; apparently made worse by treatment.

——, aged 23. Two years' history. Extensive pulmonary tuberculosis both lungs. General condition good; had recently gained 1 st. in weight. Tubercle bacilli disappeared from the sputum during treatment but reappeared later in large numbers. Total gold salt used, 1.5 g. Gold salt discontinued because of vomiting

and continuous hiccup. Prolonged anorexia. Fever, rash, and albuminuria. Three weeks after last injection, onset of hectic temperature with physical signs indicating rapid and extensive spread in the area of pulmonary involvement. No subsequent improvement. Is going steadily downhill. Result: Treatment led to extensive spread of the disease and marked general deterioration.

——, aged 36. Three years' history. Extensive chronic tuberculosis both lungs. General condition excellent; afebrile. Albuminuria. Renal function normal. Tubercle bacilli absent. Total gold salt used, 5.5 g. Moderately severe febrile reactions, nausea, and vomiting. Ten days after the last injection temperature became hectic and has remained so, with marked increase in physical signs and evidence of rapid spread of the infection. At the same time there appeared a very severe exfoliative dermatitis, apparently identical with that seen in severe arsenical poisoning. Result: Extensive spread of the disease; severe exfoliative dermatitis.

——, aged 19. Three years' history. Extensive chronic pulmonary tuberculosis of left lung; early involvement of right. General condition excellent; afebrile. Tubercle bacilli disappeared during early part of treatment, but reappeared later in increasing numbers. Total gold salt used, 7.5 g. Treatment followed by severe and prolonged reactions with fever, rash, albuminuria, and breathlessness. Severe serum sickness. After the third injection the temperature never again reached normal, the physical signs in the chest increased both in quantity and in extent, and tubercle bacilli reappeared in the sputum. Subsequent injections failed to influence the course of the disease. Serum, when given, resulted in violent reactions with rigors and collapse. The resulting situation was a very difficult one. It was obvious that the patient was going steadily downhill. It was decided to try and increase the concentration of the drug, even though, on account of the reactions, serum could not be given. Two injections of 1 g. were therefore given, with one day intervening. Four hours after the second injection there was dyspnoea, cyanosis, and blood-stained frothy sputum. Death occurred in two hours. There was no *post-mortem* examination. Result: Death.

——, aged 9 months. Tuberculous meningitis. Total gold salt used, 0.4 g. in two days. No evidence of any effect was seen. Death occurred on third day. Result: No influence detected.

In addition a case of lymphadenoma or Hodgkin's disease was treated as a control. The patient received three injections of the gold salt and no serum. There was no rise of temperature, no albuminuria, and no rash, but nausea and prolonged anorexia resulted.

ST. MARY'S HOSPITAL (PROFESSOR F. LANGMEAD).

Three cases of pulmonary tuberculosis. The early results were unfavourable and one patient died, apparently in consequence of the treatment.

——, aged 18. General condition good, but tubercle bacilli abundant. Total gold salt, 1.5 g. in four days, and over 200 c.cm. serum. Vomiting, diarrhoea, rash, fever, albuminuria, and definite serum reaction. Focal reaction in lungs. On tenth day after the last injection of gold salt, jaundice appeared and rapidly deepened. The patient died with haemorrhage from the bowels twenty-nine days after the last injection.

Necropsy found spreading tuberculosis in the lungs and recent tuberculous ulceration of the bowels. There was only one hypertrophied kidney, and that showed tubular nephritis. The kidney was not analysed for gold, but in the liver was found 0.028 g. of gold—that is, 4.75 per cent. of the total metal injected.

——, aged 32. Early disease of right apex, afebrile. Tubercle bacilli present. Total gold salt, 5 g. Fever, rash, loss of weight, albuminuria; general condition deteriorated, but is now improving, and temperature is again normal. Physical signs unchanged and tubercle bacilli still present in sputum.

——, aged 29. Peribronchial fibrosis and doubtful physical signs, but tubercle bacilli present; temperature normal. Total gold salt, 6 g. Fever, severe serum sickness, loss of weight, slight albuminuria, pain in chest, and increased expectoration. General condition at first worse, but later improving. No tubercle bacilli in sputum in last three weekly examinations, but patient developed pleurisy seven weeks after treatment was ended.

ST. THOMAS'S HOSPITAL (PROFESSOR H. MACLEAN).

Only early or slight pulmonary tuberculosis was treated, in five cases of which four had tubercle bacilli present. They were in fairly good general health, with few symptoms and generally very little pyrexia. Gold salt was given in doses of 1 g. at four to seven days' interval up to a total of 4 or 5 g. No serum was used. The reactions were slight, a little pyrexia, some albuminuria, and increase of cough. No focal pain in the chest, no anorexia. All the five cases have subsequently improved, but it is difficult to decide whether this improvement is more than would have been effected by ordinary hospital treatment. This group is, however, of great importance as a control to show that the gold salt exerts little obvious effect on the general health of patients with only mild tuberculous infections.

——, aged 27. Three months' history. No tubercle bacilli. Gold salt given, 4.5 g. No reactions except slight albuminuria persisting since fourth dose. General condition improved. *X*-ray examination showed disappearance of triangular opacity in right axilla which had suggested tuberculous infiltration.

——, aged 21. Six months' history. Tubercle bacilli present. *X*-ray examination: Disease upper third of both lungs. Very dense right apex, moderately dense left. Some fibrotic contraction right apex. Had begun to improve already with hospital treatment. Gold salt given, 4.25 g. Slight temperature reactions. Transient albuminuria for five days after fourth dose. Result: Previous rate of improvement maintained or accelerated. Final radiogram shows no change except increased contraction right apex, though radiogram taken during reaction showed increase of shadows. Tubercle bacilli present on discharge, but some evidence of fragmentation.

——, aged 28. Three months' history. Tubercle bacilli present. *X*-ray changes of medium density both lungs, occupying one-third of pulmonary fields. Gold salt given, 5.25 g. No definite reactions. Irregular pyrexia persisted. Attack of pleurisy after four weeks. Result: General condition improved; *x*-ray examination, no change.

——, aged 18. Short history. Tubercle bacilli present. *X*-ray examination: Medium opacity upper half both lungs. General condition good. Gold salt given, 5.25 g. No marked reactions. Result: General condition improved. Sputum—no tubercle bacilli on March 9th, 1925. No sputum since.

——, aged 24. Eighteen months' history. Tubercle bacilli present. *X*-ray examination: Very slight changes left apex. General condition not very good. Two doses, each followed by slight pyrexia. Rash resembling erythema multiforme two days after second injection; increased slowly during next six days; began to fade on fifteenth day. Treatment in consequence delayed, and is now being completed

UNIVERSITY COLLEGE HOSPITAL (PROFESSOR T. R. ELLIOTT).

Four cases, of which two appeared to be cured by the treatment, though the evidence was not conclusive. In two pulmonary cases with tubercle bacilli in the sputum the results were, on the other hand, definitely unfavourable.

——, aged 18. Bilateral apical infection with one year's history. Poor condition, though afebrile, and tubercle bacilli always in sputum. Total gold salt, 6.25 g. in thirty-four days, with 360 c.cm. serum. Much albuminuria, no rash, no severe serum sickness. Marked focal reaction in lungs, with pain, dyspnoea, and a serious circulatory collapse twice. Prolonged vomiting and anorexia. General condition worse and tubercle bacilli in sputum more abundant.

——, aged 29. A hopelessly rapid caseous tuberculosis, chiefly of right lung with less than six months' history. Tubercle bacilli in sputum. Patient so ill that he seemed unlikely to survive more than a couple of months. Total gold salt, 4 g. in eleven days, with 300 c.cm. serum. Slight albuminuria and no rash. Marked focal reaction in lungs with dyspnoea that persisted. Died four weeks after last gold injection, with repeated pulmonary oozings of blood.

Necropsy.—Necropsy confirmed the radiograms in showing that the caseous changes had spread rapidly into the left lung since treatment began; and the detachment of one large mass of caseous lung tissue loose within a cavity on the right side suggested that some unusually active process of destruction had been taking place. There was no tuberculosis outside of the lungs.

Disappearance of Gold from the Tissues.—Analysis found that of the total metallic gold given (40 per cent. of 4 g. salt—that is, 1.60 g.) 0.128 g., or 8 per cent., was still present in the kidneys. The percentage of gold to the weight of the kidney was 0.037. The liver retained a total of 0.012 g.—that is, barely 1/70 of the percentage found in the kidney. The lungs contained only traces that could not be measured. This rapid disappearance of the gold from the tissues where its effect was desired suggests that the salt should not be given intensively in severe cases, as advised by the Danish physicians, but at longer-spaced intervals.

——, aged 20. Tuberculous peritonitis with large encysted collection of fluid in the lower abdomen. Pleurisy at 14, with present *x*-ray evidence of fibrosis on right side. No tubercle bacilli in sputum and abdomen not explored. Condition stationary during three months' rest in hospital previous to treatment. Total gold salt, 4.5 g. in seventeen days and 80 c.cm. serum. Febrile reaction, with rash and some pain in right chest and in abdomen. The tumour had vanished by the time the last dose was given. No recurrence a month later, but still some chronic inflammation found on rectal palpation of the uterine adnexa. Patient gaining weight. Apparently a most definite improvement as the immediate result of treatment.

——, aged 14. Query localized tuberculous bronchopneumonia. Admitted for large quiescent tuberculous glands in neck, which were excised and microscoped. After anaesthetic for this operation the patient developed consolidation of left lower lobe, which took four weeks to clear up. *X* rays subsequently showed much enlargement of hilum glands and a shadow spreading outwards in the middle of the right lower lobe. The patient was under medical treatment in hospital for three months, during which time there were no tubercle bacilli in sputum, but there was continuous pyrexia and varying loss of weight. Boy seemed seriously ill when gold treatment was begun. Weight 5 st. 7 lb. Total gold, 1.25 g. in six days. Severe and prolonged rash, rise of temperature, and fall of weight to 5 st. 2 lb. No focal reaction in glands of neck. Then recovery,

with temperature thenceforward normal, and rise of weight by 2 or 3 lb. weekly to 6 st. 5 lb. on discharge from hospital. Still faint *x*-ray evidence of fibrosis in area of earlier opaqueness in right lung. The boy was cured with unusual rapidity of his lung inflammation, which was not actually proved to be tuberculous, though its appearance was clinically identical with that of hilum tuberculosis.

CARDIFF (PROFESSOR S. L. CUMMINS).

Three cases of early pulmonary tuberculosis, of which two showed definite improvement, and one, whose preliminary course of treatment has only just been completed, feels better, although he has not yet started to regain weight.

——, aged 21. Early disease involving two lobes, but only slight in density. Fair general condition. Tubercle bacilli present. Total gold salt, 4.5 g. in five weeks, and 92 c.cm. horse serum. Moderate reactions after first four doses. Sputum ceased. Tubercle bacilli vanished. Lost 2½ lb. during treatment. Has now regained this and added about 4 lb. to original weight.

——, aged 28. Definite pulmonary disease right apex, with cavitation. Tubercle bacilli present in great abundance. Total gold salt, 6.5 g. in seven weeks, and 95 c.cm. horse serum. Moderate reactions and transient albuminuria after gold salt. Severe reactions after serum. Sputum diminished and tubercle bacilli greatly reduced in number. Has lost 9 lb. during treatment. Is now feeling "as he used to before illness," but has not yet started to regain weight.

——, aged 15. Dullness and bronchial breathing upper third right lung. Tubercle bacilli present in fair numbers. Good general condition. Total gold salt, 3.25 g. in five weeks, and 36 c.cm. serum. Reaction and slight albuminuria after first dose. Intense serum sickness. Lost 3 lb. at first. Has now put on 4 lb. Is still under treatment. Appears much improved so far. No tubercle bacilli in sputum on last three examinations.

EDINBURGH (PROFESSOR SIR ROBERT PHILIP AND PROFESSOR D. MURRAY LYON).

Work at Edinburgh was not commenced until January, and while a much larger series of cases was tried than at any individual centre in London, few of these have yet reached the end of treatment. In general the results seem favourable. Serum was sparingly used, and in many cases not at all. In some tuberculous cases the Danish antituberculin serum was used alone without the gold salt, and it was not seen to have any constant influence on the temperature curve. All the patients selected were without exception afebrile at the beginning of the treatment. In the pulmonary cases tubercle bacilli were present at the commencement.

Immediate Effects of the Drug.—The first dose of 1/2 g. sanocrysin produced either very little reaction or a rise of about 2° F., the whole disturbance as a rule passing off in twenty-four to forty-eight hours. In two cases the temperature reaction to the first dose was prolonged for about ten days, a swinging temperature increasing for the first three or four days, reaching to about 103° F., and then gradually disappearing. No albuminuria or rash followed the first dose. The second dose of sanocrysin was usually followed by much larger temperature disturbance, lasting a little longer than that of the half-dose, but in most cases each subsequent dose gave rise to a smaller temperature response, until in some cases no rise occurred at all. A large number of the cases complained of loss of appetite, and in some the anorexia was very severe; vomiting has been frequent—in some cases within a few minutes after each dose, in other cases a few hours later; or, again, occurring only in the early morning each day.

Albuminuria.—A considerable quantity of albuminuria might appear after the second or third dose and remain present for several days, gradually decreasing in quantity, even without the use of serum. Renal cells and casts were present in some of the cases, but there have been no other signs of renal irritation or nephritis. A case of tuberculous kidney showed no increase in albuminuria under treatment, but after four doses treatment had to be suspended because of recurring vomiting.

Rashes.—Skin rashes have appeared in about three-quarters of the cases, irrespective of whether they have had serum or not. The rashes have varied considerably in character, from fleeting erythemas and urticarias to persistent dermatitis. In some cases the whole rash disappeared in a few hours, and in many it lasted for three or four days. The rashes were judged by an observer who had clinical familiarity with those caused by extensive tuberculin treatment to be very similar to the latter. In one pulmonary case a severe reaction has persisted for about three weeks, the whole skin being inflamed, the tissues about the face swollen, and there has been a universal desquamation. Apparently this subject had had some previous skin trouble.

Results.—In three pulmonary cases with abundant tubercle bacilli and definite *x*-ray changes there was some improvement. Sputum was lessened, but a severe rash occurred in two, and in one of these there was persistent vomiting and anorexia. In eight other cases, including lupus of the face, renal tuberculosis, and scrofulous glands of the neck, no alarming features of reaction have yet been observed.

British Medical Association.

CLINICAL AND SCIENTIFIC PROCEEDINGS.

OXFORD DIVISION.

THE second meeting of the year was held at the Radcliffe Infirmary, Oxford, on March 25th. Dr. A. W. NEILL was in the chair, and about forty members were present.

SKIN DISEASES IN CHILDHOOD.

A paper on some common skin diseases in infants and children was read by Dr. A. M. H. GRAY, physician for diseases of the skin, University College Hospital, London, and the Hospital for Sick Children, Great Ormond Street. He said that the skin of infants was very delicate, but was usually well protected by the attentions of parents and nurses, consequently bacterial infection was not very common. Streptococcal and staphylococcal infections were, however, met with. Streptococcal infection took the form of a bullous eruption, starting from the site of inoculation and spreading eccentrically. The rate of spread varied mainly with the virulence of the organism. Bullous impetigo or pemphigus neonatorum could be distinguished from syphilitic pemphigus by the symmetry of the latter, its tendency to affect the palms and soles, the presence of other types of lesion, and the malnutrition of the patient. In treating streptococcal pemphigus care must be taken to avoid loss of body heat, and large wet dressings should be avoided. The most convenient dressing was lin. calaminae to which 1 or 2 per cent. of ammoniated mercury had been added; strips of linen were soaked in this and pads of cotton-wool applied outside. Staphylococcal infection took the form of multiple boils, which were seen in weakly infants. Incision and drainage, keeping the patient warm, and care as to feeding, were the lines along which treatment should be directed.

Infants (Dr. Gray continued) were very prone to eczema of the face and scalp. Two varieties were generally recognized. The commonest form started on one or both cheeks as a red itchy patch, and friction caused the eruption to spread over the rest of the face; the eyelids and perinasal region often escaped, as they were protected by their position from friction. Later the scalp might become involved, and eczematous patches develop on the trunk and limbs. This type occurred chiefly in fat children under 1 year old, and was seen mainly in winter. It appeared to be generally associated with overfeeding. Treatment consisted in reducing the quantity of the feeds, whether breast or bottle, protection of the face from the air by a suitable mask and from friction by fixing down the hands, and by avoiding exposure to extremes of heat and cold. Coal-tar ointment applied on the mask was most generally useful; 3 per cent. crude coal tar in pasta zinci (*B.P.C.*) acted extremely well. The tar should not be applied if much sepsis was present; septic crusts could be first dealt with by 1 in 1,000 flavine-starch poultices. The other type of facial eczema usually began on the scalp and appeared to be independent of the nutrition of the child; it was thought to be primarily of seborrhoeic origin, but usually responded to the tar ointment. In some cases 1 or 2 per cent. sulphur and salicylic acid ointment was of value.

In children past the first year of life eczema was less often seen except in association with septic infection. Streptococcal infection was, however, very common. Varying forms were seen. The ordinary impetigo contagiosa started as a small thin-walled blister which rapidly ruptured, but the serum exuding from the base of the blister dried to form a crust. The lesions were usually isolated and the spread was eccentric. In some cases, however, bullae were produced and the spread might be more rapid. Lotions were the most suitable for this condition, 1 in 1,000 flavine applied on lint or linen and changed several times daily being advised. In other cases slowly spreading blisters, which flattened down and dried up in the centre, but continued to spread at the edge, were found —the so-called circinate impetigo. This was treated by